PROFILE AND OUTCOME OF DILATED CARDIOMYOPATHY IN CHILDREN
- A SHORT TERM FOLLOWUP

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CERTIFICATE

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CONTENTS

INTRODUCTION

Cardiomyopathies are defined as diseases of the myocardium associated with cardiac dysfunction [1]. They are classified by WHO as:

- Dilated cardiomyopathy
- Hypertrophic cardiomyopathy
- Restrictive cardiomyopathy
- Arrhythmogenic right ventricular cardiomyopathy

DILATED CARDIOMYOPATHY

The condition is recognized by dilatation of the left or right ventricle, or both ventricles. Dilatation often becomes severe and is invariably accompanied by hypertrophy. Systolic ventricular function is impaired. Presentation is usually with heart failure, which is often progressive. Arrhythmias, thromboembolism, and sudden death are common and may occur at any stage.

HYPERTROPHIC CARDIOMYOPATHY

This condition is characterized by disproportionate hypertrophy of the left ventricle and occasionally also of the right ventricle which typically involves the septum more than the free wall but occasionally is concentric. Typically the left ventricular volume is normal or reduced. Systolic gradients are common. Inheritance is usually by an autosomal dominant gene with incomplete penetrance. Characteristic morphological changes, usually most severe in the septum, have been described.

RESTRICTIVE CARDIOMYOPATHY

Restrictive cardiomyopathy is characterized by restrictive filling and reduced diastolic volume of either or both ventricles with normal or near-normal systolic function and wall thickness. Increased interstitial fibrosis may be present. It may be idiopathic or associated with other disease (e.g., amyloidosis; endomyocardial disease with or without hypereosinophilia).

ARRHYTHMOGENIC RIGHT VENTRICULAR CARDIOMYOPATHY

This condition is characterized by progressive fibrofatty replacement of right ventricular myocardium, initially with regional and later global right ventricular involvement. Left ventricle may be involved but with relative sparing of the septum. Clinical presentation is in the form of ventricular and atrial tachyarrhythmia, sudden death or heart failure.
Unclassified cardiomyopathies include a few cases which do not fit readily into any group like endocardial fibroelastosis, non compaction of myocardium. This includes some with minor abnormalities in which progression to overt cardiomyopathy may or may not occur. This has been referred to as latent cardiomyopathy.

SPECIFIC CARDIOMYOPATHIES

Heart muscle diseases of known cause or associated with disorders of the other system. This includes those resulting from infections, endocrine disorders, metabolic and storage diseases, nutritional

disorders, neuromuscular diseases, inflammatory, drugs-toxins, blood diseases and tumors.

Ischemic cardiomyopathy presents as a dilated cardiomyopathy with impaired contractile performance not explained by the extent of coronary artery disease or ischemic damage.

Valvular cardiomyopathy presents with ventricular dysfunction that is out of proportion to the abnormal loading conditions.

Hypertensive cardiomyopathy often presents with left ventricular hypertrophy in association with features of dilated or restrictive cardiomyopathy with cardiac failure.

Inflammatory cardiomyopathy is defined by myocarditis in association with cardiac dysfunction. Myocarditis is an inflammatory disease of the myocardium and is diagnosed by established histological, immunological, and immunohistochemical criteria. Idiopathic, autoimmune, and infectious forms of inflammatory cardiomyopathy are recognized. Inflammatory myocardial disease is involved in the pathogenesis of dilated cardiomyopathy and other cardiomyopathies, e.g., Chagas' disease, HIV, enterovirus, adenovirus, and cytomegalovirus. (2)

Metabolic cardiomyopathy includes the following categories: Endocrine, e.g., thyrotoxicosis, hypothyroidism, adrenal cortical insufficiency, pheochromocytoma, acromegaly, and diabetes mellitus; familial storage disease and infiltrations, e.g., hemochromatosis, glycogen storage disease, Hurler's syndrome, Refsum's syndrome, Niemann-Pick disease, Hand-Schüller-Christian disease, Fabry-Anderson disease, and Morquio-Ullrich disease; deficiency, e.g., disturbances of potassium metabolism, magnesium deficiency, and nutritional disorders such as kwashiorkor, anemia, beriberi, and selenium deficiency; amyloid, e.g., primary, secondary, familial, and hereditary cardiac amyloidosis, familial Mediterranean fever, and senile amyloidosis.

General system disease includes connective tissue disorders, e.g., systemic lupus erythematosus, polyarteritis nodosa, rheumatoid arthritis, scleroderma, and dermatomyositis. Infiltrations and granulomas include sarcoidosis and leukemia.

Muscular dystrophies include Duchenne, Becker-type, and myotonic dystrophies.

Neuromuscular disorders include Friedreich's ataxia, Noonan's syndrome, and lentiginosis.

Sensitivity and toxic reactions include reactions to alcohol, catecholamines, anthracyclines, irradiation, and miscellaneous. Alcoholic cardiomyopathy may be associated with a heavy alcohol intake. At present we cannot define a causal versus a conditioning role of alcohol or apply precise diagnostic criteria.

Peripartal cardiomyopathy may first manifest in the peripartum period. This is probably a heterogeneous group.

DILATED CARDIOMYOPATHY

Idiopathic dilated cardiomyopathy (DCM) refers to congestive cardiac failure secondary to dilatation and systolic dysfunction (with or without diastolic dysfunction) of the ventricles (predominantly left) in the absence of congenital, valvular, or coronary artery disease or any systemic disease known to cause myocardial dysfunction. DCM is the most common type of heart muscle disease in children. Varying degrees of ventricular hypertrophy are also present.

PATHOPHYSIOLOGY

Injury to the myocardial cell is the initiating factor that leads to cell death. If considerable cell loss occurs, the myocardium fails to generate enough contractile force to produce adequate cardiac output. This results in the activation of compensatory mechanisms, including the renin-angiotensin-aldosterone system, sympathetic stimulation, antidiuretic hormone production, release of atrial natriuretic peptide, tumor necrosis factor (TNF)-a, and mechanical factors, such as increased end-diastolic stretch on the ventricle. These compensatory mechanisms help to maintain cardiac output in the initial phase; however, as myocardial damage progresses, persistent and excessive activation can be detrimental to cardiac function, leading to overt congestive heart failure.

Over-stretching of the ventricles causes myocardial thinning, cavity dilation, secondary valvular regurgitation, and compromised myocardial perfusion. The resulting subendocardial ischemia perpetuates myocyte damage.

Myocardial remodeling is an important contributor to worsening heart failure. Lost myocyte cells are replaced with fibrous tissue, thereby decreasing the compliance of one or more ventricles and adversely affecting performance. Aldosterone, angiotensin II, catecholamines, endothelins, and mechanical factors, such as excessive myocardial stretch and ischemia, have been identified as mediators of remodeling.

CAUSES

Various factors have been identified as causes of myocardial damage. However, in the vast majority of patients, no specific etiology is demonstrable (idiopathic). Three major factors have been implicated in the pathogenesis of myocardial damage in DCM: preceding viral myocarditis, autoimmunity, and underlying genetic predisposition. According to the Pediatric Cardiomyopathy Registry, cardiomyopathies can be grouped into five categories based on the specific genetic cause of the

disease: 1) myocarditis and other viral infections (27%), 2) familial inherited cardiomyopathies (24%), 3) neuromuscular disorders associated with cardiomyopathy (22%), 4) metabolic disorders (16%) and 5) syndromes associated with cardiomyopathy (10%).

VIRAL MYOCARDITIS

Active myocarditis is identified in 2-15 % of patients. Epidemiologic, serologic, and molecular studies have detected evidence of enteroviral infection, in particular coxsackievirus B, in 20-25% of patients. Recent evidence implicates various other viruses. In fact, the most common associated viruses appear to vary over time. (3, 4)

Currently, no methods can be used to distinguish cardio virulent strains of enteroviruses from those that are not virulent. Furthermore, the presence of a virus a patient with DCM does not necessarily establish a causal relationship. Demonstration of viral DNA or RNA by polymerase chain reaction (PCR) is a more reliable method for revealing viral myocarditis. Unfortunately, obtaining myocardial tissue is invasive. The exact mechanism of myocardial damage (rapid destruction or a long-term slowing of cardiomyocyte function) also remains unclear.

AUTOIMMUNITY

Animal studies have shown that DCM is an autoimmune disease in genetically predisposed strains of mice. Approximately 30-40% of adult patients with DCM have organ-specific and disease-specific autoantibodies. The absence of these antibodies in the remaining patients may be related to the stage of disease progression. It has been postulated that an insult such as viral myocarditis initiates an autoimmune process with superantigen-triggered immune responses, resulting in massive T-lymphocyte activation and myocardial damage.

GENETIC PREDISPOSITION

Genetic causes account for 25-50% of DCM cases. The role of genetic factors is exemplified by the studies on familial DCM. (5, 6) Patients with familial DCM have an increased frequency of human leukocyte antigen HLA-DR4. The frequency of HLA-DQA1 0501 alleles has been reported to be significantly higher in patients with idiopathic DCM. (7)

Autosomal dominant and recessive inheritance, X-linked transmission, and polygenic and mitochondrial inheritance have all been documented. Mitochondrial myopathies may be due to mutations of either nuclear DNA or mitochondrial DNA. Mitochondrial abnormalities leading to DCM involve enzymes of the electron transport chain (nuclear DNA) or enzymes of fatty acid oxidation (mitochondrial DNA)

Summary of Genetic Loci and Disease Genes for Familial Dilated Cardiomyopathy

Clinical Pattern	*Identified Genetic Loci*	*Identified Disease Genes*
Autosomal dominant (AD)	10q21-10q23, 9q13-q22, 1q32, 15q14, 2q31, 1q11-21	Actin, desmin, lamin
AD with conduction defect	1p1-1q1, 3p22-3p25	
X-linked (XL)	Xp21	Dystrophin
XL cardio-skeletal (Barth syndrome)	Xq28 (gene G4.5)	Tafazzin

Mutation analysis: Mutation screening of the exons that code for actin, β myosin heavy chain (*MYH7* gene), cardiac troponin T (*TNNT2* gene), phospholamban (*PLN* gene), titin, αβ-crystallin, and the cardio-specific exon of metavinculin (*VCL* gene) could be helpful in detecting some forms of familial DCM.

Neuromuscular diseases associated with cardiomyopathy include those that affect the nerve or skeletal muscles. These include muscular dystrophies (i.e. Duchenne and Becker), congenital myopathies, metabolic myopathies, and ataxias (i.e. Friedreich Ataxia).

Inborn errors of metabolism consist of numerous infiltrative storage diseases, abnormal energy production, biochemical deficiencies and disorders related to toxic substances accumulating in the heart. This category also includes mitochondrial abnormalities (i.e. MELAS, MERRF, respiratory chain diseases, mitochondrial myopathies), fatty acid oxidation defects (carnitine deficiency, VCHAD, LCHAD, LCAD, MCAD), Pompe disease and Barth syndrome.

Barth syndrome, a rare and relatively unknown genetically linked cardiac disease, has been known to cause dilated cardiomyopathy. This syndrome usually affects male children in their first year of life.

Malformation syndromes are characterized by minor and major physical abnormalities with distinctive facial features. Noonan syndrome is the most common form associated with pediatric cardiomyopathy. Common symptoms include short stature, webbed neck, wide set eyes, low set ears and extra skin folds.

Other causes for acquired cardiomyopathy include: 1) cardiovascular conditions (i.e. Kawasaki disease, congenital heart defect, hypertension, cardiac transplantation or surgery), 2) infectious or inflammatory diseases, 3) immunologic diseases (i.e. HIV), 4) obesity or dietary deficiencies, 5) toxin reactions (i.e. drug, alcohol, radiation exposure), 6) connective tissue and autoimmune diseases, 7) endocrine diseases and 8) pregnancy related complications. Persistent rhythm disturbances or abnormalities of the coronary arteries, either congenital or acquired, can lead to myocardial dysfunction.

PRESENTATION OF CARDIOMYOPATHY

Onset is usually insidious but may be acute in as many as 25% of patients, especially if exacerbated by a complicating lower respiratory infection. People with different stages of disease have varying combinations of symptoms. Cough, poor feeding, irritability and shortness of breath are usually the initial presenting symptoms. Pallor, sweating, easy fatigability, failure to gain weight, and decreased urine output may be observed. Wheezing may be an important clinical sign, suggesting congestive heart failure manifestation in infants. Chest pain, palpitations, orthopnea, hemoptysis, frothy sputum, sudden death, abdominal pain, syncope, and neurologic deficit are other symptoms at presentation (20%). Cardiomegaly that is incidentally detected on a chest radiograph or an arrhythmia that is incidentally detected on an ECG may be the basis for initial cardiac referral.

Approximately 50% of patients with dilated cardiomyopathy (DCM) have a history of preceding viral illness. A detailed family history for familial cardiomyopathy is revealing in as many as 25% of cases.

Children with cardiomyopathies of a metabolic nature may have additional symptoms of hypoglycemia, metabolic acidosis or neurological abnormalities such as hypotonia and encephalopathy.

PHYSICAL FINDINGS

In a patient with established disease, features of congestive heart failure are dominant. The infants or young children with dilated cardiomyopathy often have tachypnea, tachycardia with weak peripheral pulses, and have cool extremities and hepatomegaly. Blood pressure is low with a decreased pulse pressure. In extreme cases, patients may present in shock. Older children may show dependent edema, elevated jugular venous pulses, and fine basal crepitations in the lungs.

Major cardiac findings include cardiomegaly, quiet precordium, tachycardia, gallop rhythm (S3 and/or S4), accentuated pulmonary component, and murmurs of mitral and tricuspid regurgitation. Murmurs may be inconspicuous initially if the patient presents with acute heart failure. Infants often present with predominantly respiratory signs and, in the absence of a precordial heave or prominent murmur, the underlying cardiac disease may remain undiagnosed until cardiomegaly is detected on a chest radiograph.

EVALUATION & DIAGNOSIS

Noninvasive

- Electrocardiogram (ECG)

- Echocardiogram
- Chest X-ray
- Holter Monitor
- Blood tests

Invasive

- Radionuclide Ventriculogram
- Cardiac Catheterization
- Right ventricular endomyocardial biopsy

CHEST RADIOGRAPHY

Chest radiography reveals cardiomegaly with a prominent left ventricular apex and prominent pulmonary artery segment. Elevation of left main bronchus reflects dilation of the left atrium. This can result in compression of the left lower lobe bronchus when combined with a dilated pulmonary artery, leading to collapse of the left lower lobe of the lung. Pulmonary venous congestion and frank pulmonary edema are often evident. When present, pleural effusion is better appreciated in the erect and lateral decubitus films. Massive cardiomegaly resembling pericardial effusion is the hallmark of established disease. Rarely, in fulminant cases, cardiomegaly may not be prominent because the ventricle has not had time to dilate despite the presence of features of pulmonary edema.

ELECTROCARDIOGRAPHY

ECG changes are usually nonspecific with sinus tachycardia, downward frontal plane QRS axis, left atrial enlargement, left ventricular hypertrophy, deep Q waves with ST segment depression, and tall T waves in leads I, aVL, V_5, V_6 (the latter reflect left ventricular volume overload). In more advanced disease, right axis deviation, right atrial enlargement, and right ventricular hypertrophy are seen secondary to pulmonary hypertension.

The main role of ECG is to detect evidence of myocardial ischemia (pathologic Q waves with ST elevation and T-wave inversion in leads I, aVL, V_5, V_6) that might point to anomalous coronary artery as the etiology of the cardiomyopathy. A segmental myocarditis may result in ECG features of myocardial infarction.

Cardiac arrhythmias, such as supraventricular/ventricular ectopy or tachycardia, may be revealed. These might indicate an underlying myocarditis or cardiomyopathy; however, if sustained, the arrhythmia may be the cause of the cardiomyopathy rather than the result (i.e., tachycardia-mediated cardiomyopathy).

HOLTER MONITOR OR 24 HOUR TAPE

An external device is worn for 24-72 hours which continuously records the heart rhythm. It identifies any irregular heart rhythms commonly associated with dilated cardiomyopathy.

ECHOCARDIOGRAPHY AND DOPPLER STUDIES

These form the basis for the diagnosis of dilated cardiomyopathy (DCM) in most patients. Marked dilation of the left ventricle with global hypokinesia is the hallmark of the disease. Left ventricular fractional shortening is usually less than 25% (ejection fraction <50%). Left ventricular walls are thin and areas of dyskinesis may be observed. The left atrium is also dilated, and mitral valve leaflets show sluggish movement; the anterior leaflet does not appose to the interventricular septum, giving an increased E point septal separation on the M-mode pictures. The M-mode also clearly reveals the limited excursions of the anterior and posterior leaflets during diastole.

Doppler studies show varying degrees of mitral regurgitation secondary to left ventricular dilation and possible papillary muscle dysfunction. Mitral regurgitation is more prominent in follow-up studies after commencing therapy when the cardiac output has improved. Left ventricular ejection parameters show decrease in peak velocity and peak acceleration, prolongation of the pre-ejection period, and decrease in ejection time. These flow measurements are dependent on loading conditions. The dilatation of the mitral valve ring and the altered shape of the left ventricle cavity, which leads to change in the direction of the papillary muscles, are used to explain the secondary mitral regurgitation seen in a large proportion of children with DCM. Tissue Doppler studies have recently been reported in children with DCM.

Long-standing cases show evidence of pulmonary hypertension in the form of right ventricular dilation and hypertrophy and tricuspid regurgitation. Tricuspid regurgitation and pulmonary regurgitation velocities give an estimate of the pulmonary artery systolic and diastolic pressures respectively. Occasionally, thrombi can be visualized in the left ventricular apex and in the left atrium. Pericardial effusion also may be present.

Echocardiography can exclude other heart diseases, both congenital and acquired. Cardiomyopathy secondary to severe aortic stenosis, coarctation of aorta or congenital mitral valve dysplasia, and anomalous left coronary artery arising from pulmonary artery (ALCAPA) are the major differential diagnoses. At times, identifying cardiomyopathy secondary to congenital mitral regurgitation (dysplastic mitral valve without stenosis) is difficult, but the abnormal anatomy of the mitral valve leaflets should help. The echo-dense papillary muscles and the dilated proximal right coronary artery and continuous retrograde flow of blood into the origin of pulmonary artery all direct the attention of the cardiologist to ALCAPA, a potentially treatable condition that mimics DCM.

RADIONUCLIDE IMAGING

First-pass test and multiple gated acquisition (MUGA) scan help to measure the left and right ventricular stroke volumes and cardiac outputs. They are also helpful in documenting dyskinetic segments in the ventricular walls. Although theoretically superior to echocardiographic measurements, their practical application is limited because of cost, lack of standardization and non reproducibility, especially in children.

CARDIAC CATHETERIZATION AND ANGIOGRAPHY

At present, preparation for cardiac transplant and need for myocardial biopsy are the main indications for performing the procedure. Usual findings include elevated filling pressures in all the cardiac chambers (especially the left ventricle), elevated pulmonary wedge pressure, and reduced cardiac output and stroke volume. Mixed venous oxygen saturation and reduced arterial saturation reflect low cardiac output and pulmonary edema. Pulmonary and systemic vascular resistances are elevated. With end-stage disease, the peak systolic left ventricular and aortic pressures drop.

MYOCARDIAL BIOPSY

At present, preparation for cardiac transplant and post-transplant follow-up monitoring for rejection are the main indications for biopsy. If facilities are available, molecular or metabolic studies can be additional indications for academic and research purposes. Rarely, suspected metabolic diseases (isolated myocardial carnitine deficiency, rare forms of glycogen storage disease, fatty acid oxidation defects) or persistent myocarditis might require biopsy for confirmation.

Specimens should be subjected to both light and electron microscopy. PCR and metabolic studies should be performed when indicated. Histologic features are nonspecific in most patients and include myocardial cell loss with varying degree of necrosis and fibrosis. In presence of myocarditis, lymphocytic infiltration of varying degree is also present (Dallas criteria). PCR has been used to aid the detection of viral antigens in myocardial tissue in patients with DCM. Studies have revealed an association between viral antigens and DCM. However, a proportion of the studies gave negative results.

LAB STUDIES

Full blood counts, erythrocyte sedimentation rate, and C-reactive proteins may show evidence of acute inflammation in the presence of active myocarditis.

Similarly, creatine kinase–myocardial fraction may be elevated. Rising titers of specific viral-neutralizing antibodies in the serum and positive viral cultures from nasopharyngeal or stool swabs may suggest a viral etiology; however, this does not necessarily mean a cause-and-effect relationship.

Serum carnitine levels (total and free) are low when the disease is due to systemic carnitine deficiency.

Arterial blood gas (ABG) analysis reveals early stages of mild respiratory alkalosis and, later, mild hypoxemia secondary to pulmonary edema. In advanced disease, mixed acid-base disturbances with metabolic acidosis indicate the need for intravenous inotropes and ventilatory assistance.

TREATMENT & MANAGEMENT

In general, the aim of medical therapy for a child with dilated cardiomyopathy is to 1) control symptoms of congestive heart failure, 2) improve heart function and contracting ability and 3) prevent complications such as blood clots or arrhythmias.

A multidisciplinary approach is a must for optimum management and should include the following:

- Pediatric cardiologist
- Pediatric cardiothoracic surgeon
- Pharmacist
- Dietitian and nutritionist
- Pediatrician or family physician
- Occupational therapist
- Psychologist
- School teacher
- Specialist nurse

Diet and Activity

Dietary requirements are high because of the catabolic state, recurrent infections, increased muscle activity, and need for rapid growth. Powerful diuretics have largely obviated the need for stringent restrictions on salt and fluid intake. Enforced bed rest is impractical and probably unnecessary. Infants might need intravenous alimentation for relief from feeding activity. Activity to the limit of tolerance should be allowed and encouraged. In patients with chronic illness, regular graded exercise has been shown to improve effort tolerance and quality of life.

DRUG THERAPY

Medical therapy is largely directed at the symptoms and is aimed at the underlying heart failure.

Diuretics, digoxin, angiotensin converting enzyme (ACE) inhibitors, beta receptors blockers, Angiotensin II receptor blockers, Aldosterone inhibitors, Vasodilators all are tired in the treatment of dilated cardiomyopathy. ACE inhibitors prevent further dilation or enlargement of the ventricle. This directly increases the chance for long-term survival by reducing the stress on the heart muscle. Anticoagulant medications are indicated in severe left ventricular dysfunction to prevent thrombus formation and embolism.

If the disease is diagnosed at an advanced stage, critically ill patients may require immediate lifesaving measures like mechanical ventilation and administration of medications intravenously (i.e. dobutamine, dopamine) to improve blood pressure and heart function. Once the patient has stabilized, therapy involving oral medication, implantable devices, and surgery or heart transplantation will be considered.

OTHER TREATMENT MODALITIES

An implantable cardioverter defibrillator (ICD) is indicated in patients who survive sudden cardiac death and in those patients at risk of death due to severe arrhythmias. Heart resynchronization therapy (biventricular pacing) is a type of pacemaker device that ensures activation of different portions of the heart at the same time, resulting in more efficient heart contractions. Heart transplantation may be necessary for patients in the advanced stages of heart disease who have a poor response to medical treatment and in whom the underlying problem could not be reversed or modified. Some patients with severe heart failure awaiting a heart transplant may be treated with a ventricular assist device. This is a mechanical pump that assists the failing heart that is implanted in open heart surgery.

COMPLICATIONS

- Congestive heart failure
- Pneumonia
- Cardiac arrhythmias (supraventricular and ventricular)
- Infective endocarditis
- Thromboembolism
- Venous thrombosis
- Cardiac cirrhosis
- Post-transplant complications
- Sudden, unexplained death

GENETIC COUNSELING

Family members should be screened with ECG and echocardiography to detect asymptomatic cases. Identifying who may be affected is important for family planning as well as assessing the risk to relatives and siblings. Since cardiomyopathy can be inherited and present without any signs or symptoms, it is recommended that all first-degree relatives of a patient (parents, siblings, and children) be screened. It is also advisable to screen grandparents, aunts, uncles, and cousins. This is especially the case if there is a family history of sudden infant death or sudden cardiac arrest.

LONG TERM PROGNOSIS

The long-term outlook of pediatric cardiomyopathy continues to be unpredictable because it occurs with such a wide spectrum of severity and outcome. Although presently there is no cure for cardiomyopathy, some symptoms and complications can be managed and controlled with medication and implantable devices. Some children will stabilize with proper treatment and are able to lead normal or nearly normal lives with some restrictions on exercise capacity. A heart transplant may solve the problem but at the expense of other possible medical complications. If a treatable cause is discovered, prognosis is better. In DCM with no obvious detectable etiology, outcome depends on severity of myocardial dysfunction, improvement during the first year after onset, compliance to therapy, and availability of timely transplant.

Mortality for DCM is highest in the first year after diagnosis with a reported survival at 1 and 5 years after first presentation of 79% and 61% respectively. (8) Early deaths are principally caused by severe heart failure. Some late deaths are sudden, presumably due to arrhythmia, in children who fail to recover to normal ventricular function. While it is accepted that the risk of mortality is high there is less agreement as to predictors of poor outcome. Failure of improvement or deterioration in shortening fraction, ventricular arrhythmias, detection of mural thrombus, presentation at age >2years, endocardial fibroelastosis and left ventricular end diastolic pressure >20mmHg have all been put forward as adverse prognostic factors. (8, 9, 10, 11)

The prognosis of childhood DCM is variable and probably reflects the heterogeneous etiology of the disease. (11) In children with DCM, approximately 35% recover completely, 35% stabilize and the remaining may progressively worsen. Children with DCM are more prone to congestive heart failure and have a higher rate of heart transplantation compared with other forms of cardiomyopathy. However, improved medical therapy may eventually change this scenario.

REVIEW OF LITERATURE

Anita arola, et al (11) from Finland studied the outcome of idiopathic DCM and prognostic indicators in Finnish children. Records of 62 children were retrospectively analyzed. Of the 62 patients 32(52%) were males. In their study 10(16%) had familial cardiomyopathy. A recent viral illness was reported in 29(47%) patients. 45(73%) patients presented with congestive heart failure. LVH and LAH were found in 62% and 45% of cases. Low voltage QRS complexes were present in 10(17%) cases and prognostic importance. Vascular congestion on initial chest radiograph had poorer prognosis. At the end, only 16% patients recovered and 27% had residual disease. Histologic evidence of endocardial fibroelastosis, clinical signs of right ventricular failure at presentation, and the need for anticoagulative therapy during follow-up, the last an expression of a severely impaired left ventricular systolic function, appeared to be significant predictors of long-term outcome. Final Conclusion given was the outcome of children with IDCM still remains poor. However, a group of patients, mainly infants, make a full recovery. Adolescent male patients as well as infants suffering from endocardial fibroelastosis with persisting symptoms of congestive heart failure after initiation of medical therapy tend to have the poorest outcome.

Shyam S Kothari, et al (12) from All India Institute of Medical Sciences studied the clinical course and prognosis of dilated cardiomyopathy in Indian children. They retrospectively reviewed the records of 82 children with DCM from 1992 to 2001. Of the 82 children 50 were males. Family history of DCM was present in 3.5% of cases. History suggestive of antecedent viral infection was found in 25(30.5%) patients. LVH and ST-T changes were present in 78% and 39% of cases respectively. Cardiomegaly was present in all cases with mean CTR 66%. They found that mortality was high in infants diagnosed with DCM. They have reported 59% of children improved with treatment. Among the prognostic variables age at diagnosis, cardiothoracic ratio and ratio of LVED/LV PWT only came significant. They have concluded saying that children with DCM pursue a variable course. Diagnosis in infancy, larger cardiothoracic ratio, and a higher LVED/PW thickness ratio are associated with poor prognosis. More than half the patients diagnosed beyond infancy improve or recover. Further characterization of prognostic variables is warranted.

Jeffrey A. Towbin, et al. (13) studied the incidence, causes, and outcomes of dilated cardiomyopathy in children in United States. It was a population based longitudinal study. A total of 1426 children were studied. They reported overall incidence of 0.57 cases per 100000 per year. The incidence was higher in boys and in infants. Age younger than 1 year was the most common age at diagnosis of DCM (n = 591 [41%]). Congestive heart failure at diagnosis was present in 71% and 27% had class IV heart failure. The cause of DCM was identified in 34% of patients and the most common causes were myocarditis (46% [222/485]) and neuromuscular disease (26% [125/485]). Familial DCM was found in 14% of patients. Among the 54 patients with inborn errors of metabolism, the largest subgroups were mitochondrial disorders (46% [20/54]), Barth syndrome (24% [13/54]), and primary or systemic carnitine deficiency (11% [7/54]). Malformation syndromes were the least common cause of DCM. Children with DCM had 1-year survival of 87%, 2-year survival of 83%, 5-year survival of 77%, and 10-year survival of 70%. Age at diagnosis, Cause, CHF at diagnosis, and fractional shortening *Z* score were significant predictors of outcome. Fractional shortening was the only independent echocardiographic risk factor. Conclusions arrived was, DCM is a diverse disorder with outcomes that depend largely on cause, age, and heart failure status at presentation. Race, sex, and age affect the incidence of disease. Most children do not have a known cause of DCM, which limits the potential for disease-specific therapies.

Piers E. F. Daubeney, et al (14) conducted population based study on Clinical Features and Outcomes of Childhood Dilated Cardiomyopathy in Australia from 1987 to 1996. There were 184 subjects with DCM. Childhood dilated cardiomyopathy is most common during the first year of life and is associated with significant morbidity and mortality. At presentation, 90% of cases had signs and symptoms of congestive heart failure, and sudden death was the presenting symptom in 4%. The median age of the 9 cases whose initial symptom was sudden death was 2 months (range 8 days to 11 months). Familial cardiomyopathy was identified in 14.7% of subjects, a metabolic or mitochondrial disease in 8.9%. A potential viral contribution (lymphocytic myocarditis or positive viral identification) was identified in 68.2% of case subjects (most commonly coxsackievirus or adenovirus). Age >5 years at presentation, familial dilated cardiomyopathy, a lower fractional shortening *z* score at presentation, and failure to increase fractional shortening *z* score from presentation. At follow-up, 78 (44.6%) of 175 cases have no symptoms and are not taking any cardiac medication. Early mortality is high in childhood dilated cardiomyopathy, but the clinical status of long-term survivors is good was the conclusion given.

Anita Khalil, et al (15) from Maulana Azad Medical College studied the clinical profile, treatment and outcome of DCM in children. 25 children were evaluated for their clinical profile and comparative efficacy of beta blockers and ACE-inhibitors in children with dilated cardiomyopathy. All of them presented with congestive failure. Electrocardiograms revealed tachycardia in all. There was increase in LVDd and LVDs (left ventricular diameters in diastole and systole) and depression in fractional shortening (FS) in all the patients. Antibodies to Coxsackie B virus were present in 16%. No one had antibodies against HIV. , 5 (20%) patients expired, one of refractory congestive heart failure (Group II) and the remaining 4 (Group I) expired due to arrhythmias. They have concluded that arrhythmias form an important mode of death and ACE-inhibitors were better as a mode of therapy.

C J McMahon, et al (16) at Texas children's hospital, USA conducted a prospective clinical study to evaluate echocardiographic predictors of adverse clinical events in children with dilated cardiomyopathy. Conclusions of the study were children with DCM have significantly lower TD (tricuspid early diastolic velocity) velocities than normal controls. In such cases, lower LVEF (< 30%) is more sensitive but less specific than lower tricuspid Ea velocities (< 8.5 cm/s) in predicting which patients are at risk of hospitalization, transplantation, or death.

Vitor Manuel Pereira Azevedo, et al (17) in his study to determine echocardiographic predicting factors of death in children with idiopathic DCM retrospectively analyzed records of 148 children. 81(54.7%) were females and 73% were less than 2 years old. 80.4% patients had NYHA class III-IV at presentation. 60(40.5%) children recovered fully. On analysis they found worsening of mitral and tricuspid insufficiencies were markers of death. Conclusion was patients with a progressive increase in LAD/Ao, a reduction in LVEF, progressive worsening of mitral insufficiency should be considered for early heart transplantation.

A matitiau, et al (18) from Harvard Medical School, Boston studied relation of outcome to left ventricular mechanics, hemodynamics, and histology at the time of presentation infantile dilated cardiomyopathy. In their study with 25 children 45% recovered completely, 25% survived with persistent left ventricular dysfunction and 30% died. Severely depressed left ventricular ejection fraction and spherical left ventricular shape at presentation were associated with poorer outcome. They have concluded as histological and echocardiographic features can be used to identify patients at high risk for death. Recovery of function was often rapid, but continued improvement may be seen for as long as 2 years.

Anna E. Tsirka, MD, et al (19) from Missouri, USA have reported improved outcomes of pediatric dilated cardiomyopathy with utilization of heart transplantation. Retrospective study of reports of 91 children was done. 58(64%) were male gender and congestive heart failure was present in 72(79%) of children at presentation. 60% cases were found to be idiopathic and familial DCM in 9%. Within the first year after diagnosis, 90% of the transplantations and 64% of the deaths occurred. Although the majority (57%) of children who underwent recovery of LV systolic function did so in the first year, a substantial proportion returned to normal up to six years after presentation. Actuarial survival of the children from the time of diagnosis was 90% at one year (82 of 91) and 83% (76 of 91) at five years. Female gender ($p = 0.02$), age <1 year ($p = 0.002$), age >12 years ($p = 0.006$), lower LVSF *z* scores ($p = 0.006$), and higher LVESD *z* scores ($p = 0.03$) as variables at presentation significantly associated with death or transplantation. Concluded saying that this study illustrates the improvement of survival in infants, children, and adolescents diagnosed with pediatric DCM offered by routine use of heart transplantation.

Inas Abdullsattar Saad (20) from Cairo University, in his study on: Natural History and Predictors of Prognosis Idiopathic Dilated Cardiomyopathy in children has reported a gender distribution of 65.5% female and 35.5% male among 55 children with DCM. Cardiomegaly was noted on chest radiography in 90% of our patients, but only 56.3 % had increased lung vascularity. ST segment and T wave changes were seen on electrocardiogram in 69% of cases. 69% had LVH, 13% had low voltage, and 14.5% had arrhythmias. younger age of presentation, higher z-score of inter-ventricular septum and left ventricle posterior wall dimension in diastole are predictors for favorable outcomes, and left ventricular end diastolic dimension of high z-score is related to unfavorable outcomes.

STUDY JUSTIFICATION

Dilated cardiomyopathy (DCM) is the most common childhood cardiomyopathy and is associated with considerable morbidity and mortality. Though less common, DCM is a serious disorder. The natural history of DCM has been studied for over 2 decades, but remains inadequately characterized. Previous studies from other countries have provided important epidemiological information on DCM in children. Data on predictors of adverse clinical outcome in children with dilated cardiomyopathy remain limited despite several studies over the past two decades. Risk stratification of children with DCM is important to plan management and to predict morbidity and mortality.

With the availability of heart transplantation in India, profile and prognostic information for Indian children with dilated cardiomyopathy is clearly needed. Hence it was planned to study the profile of DCM and to characterize the prognosis of DCM in a relatively large number of children seen at our tertiary institution.

AIM OF THE STUDY

TO STUDY

1. The clinical profile of dilated cardiomyopathy in children

and

2. The risk factors predicting the short term outcome of dilated cardiomyopathy in children

SUBJECTS AND METHODS

METHODOLOGY

STUDY DESIGN: Descriptive study.
STUDY PLACE: Institute of Child Health and Hospital for Children.
STUDY PERIOD: October 2005 to June 2007.
STUDY POPULATION: Children admitted/attending ICH&HC.

INCLUSION CRITERIA:

- All cases of DILATED CARDIOMYOPATHY defined as:
- Left ventricular ejection fraction < 40%
- Left ventricular end diastolic dimension > 2SD above normal.

EXCLUSION CRITERIA:

All secondary causes of ventricular dysfunction

- Structural heart diseases
- Hypertension
- Arrhythmias
- Neuromuscular diseases
- Coarctation of aorta
- Coronary artery anomaly
- Kawasaki's disease
- Systemic diseases

SAMPLE SIZE:

All children with dilated cardiomyopathy satisfying case definition during study period.

MANOEUVER

The diagnosis of DCM was based on clinical examination and echocardiographic evidence of systolic ventricular dysfunction (left ventricular ejection fraction < 20%) [1]. Secondary forms of myocardial disease, such as those resulting from neuromuscular diseases, systemic diseases, hypertension, arrhythmias, structural abnormalities of heart, coronary artery abnormalities, were excluded. All patients who fulfilled the criteria for diagnosis of DCM were enrolled after informed consent.
A detailed history was taken to determine age, gender, onset, presenting symptoms and progression of symptoms, any upper respiratory or gastrointestinal illness within 3 months of presentation, previous hospitalization and medication, family history of similar complaints in any first degree relatives.

All of them underwent thorough clinical examination and their vital parameters, anthropometric parameters, general examination and system examination findings were recorded. Based on history and examination their cardiac status was graded according to New York Heart Association classification. Cardiac evaluation included chest radiograph, electrocardiogram and echocardiogram with Doppler studies. The laboratory studies included estimation of serum calcium and viral markers for coxsackie B virus and HIV infection. All of them received the same treatment for cardiac failure and complications if developed.

The date of initial presentation was defined as the first documentation of left ventricular dilatation and dysfunction. Follow up was by repeated clinical and echocardiographic examination.

The following data were recorded for each patient: age, gender, symptoms at presentation, duration of symptoms, history suggestive of viral illness at the onset, family history of heart disease or of sudden death, New York Heart Association (NYHA) functional class, cardiothoracic ratio and pulmonary congestion on chest X-ray, left ventricular hypertrophy (LVH) by age-dependent voltage criteria, and ST–T changes and arrhythmias on ECG, serologic markers for coxsackie B virus and HIV infection and serum calcium. In addition, several echocardiographic variables, including left ventricular dimensions, ejection fraction, fractional shortening, LV diastolic dysfunction, pulmonary hypertension, presence of mitral regurgitation and LV clot, and left ventricular end-diastolic dimension/posterior wall (LVED/PW) thickness ratio were analyzed.

At the end of study, patients were divided into three groups based on the outcome namely, improved or cured (group I), not improved (group II), worsened or died (group III). Patients with improved clinical status and an increase in the ejection fraction >5% were defined as improved (group I). Of these, patients with normalization of left ventricular dimensions and no clinical symptoms were labeled as cured. No change or ≤5% change in the ejection fraction was considered as unchanged (group II). Clinical worsening and/or decline in the ejection fraction >5% was classified as worsened (group III). (11, 12) For statistical analysis outcome was taken as those with favorable outcome (group I) and those with poor outcome (group II& III).

STATISTICAL ANALYSIS

1. Demographic parameters of dilated cardiomyopathy in children
2. To associate various parameters to outcome, univariate analysis was done to arrive at odds ratio (OR) with 95% confidence interval.
3. To associate how far individual factors contribute independently for short term outcome, multivariate analysis was done.

OBSERVATIONS

The results of 55 children with dilated cardiomyopathy are as follows.
The following is the demographic profile of children with DCM

Table 1:
Demographic profile of children with DCM

S.No.	*Characters*		*Number*	*Percentage*
1	Age (in months)	0 – 12	23	41.82
		> 12	32	58.18
2	Sex	Male	27	49.09
		Female	28	50.91
3	NYHA CLASS	II	4	7.27
		III	26	47.27
		IV	25	45.45
4	Preceding viral infection		14	25.45
5	Family history		3	5.45
6	CCF at presentation		51	92.73
7	Pulmonary congestion		17	30.91
8	Feeding difficulty		13	56.5
9	Anasarca		11	20

About 41.9% cases were less than 12 months old. No gender difference was present. 92.7% had congestive cardiac failure at presentation with NYHA class III-IV. Family history was present in 3 children (5.45%), all were siblings. 56.5% of infants presented with feeding difficulty as presenting complaint. Edema in the form of anasarca was present in 20% of patients (Table 1).
The following is the mean and standard deviation for heart rate, respiratory rate and cardiothoracic ratio of children with DCM.

Table 2:
HR, RR, CTR characters of children with DCM

SI No.	*characters*	*Mean*	*SD*

1	Heart Rate(HR)	147.53	17.86
2	Respiratory rate(RR)	49.85	12.82
3	Cardio thoracic ratio(CTR)	63.07	4.46

All of them had tachycardia and tachypnea for their age and Cardiomegaly at presentation. (Table 2)
The following is the Electrocardiography profile of children with DCM

Table 3:
Electrocardiography profile of children with DCM

SI No	***Characters***		***Number***	***Percentage***
1	Chamber enlargement	LVH+LAE	10	18.18
		LVH	33	60
2	ST-T Changes		28	50.91
3	Low Voltage Complex		10	18.18
4	Rhythm disturbance		11	20

Left ventricular hypertrophy was present in 60% of patients. Rhythm disturbances were atrial premature depolarization in 4 cases, ventricular premature depolarization in 3 cases, atrioventricular block in 2 cases, left bundle branch block in a case and left anterior fascicular block in a case. (Table 3)
The following is the Laboratory profile of children with DCM

Table 4:
Laboratory profile of children with DCM

SI No	***Characters***	***Number***	***Percentage***
1	Serum calcium normal	53	96.36
2	Serology for coxsackie B	7	12.73
3	Serology for HIV	3	5.45

Serology showed positive for coxsackie B infection in 7 (12.73%) of cases. Three of them were retro virus positive. (Table 4)
The following is the Echocardiography profile of children with DCM

Table 5:
Echocardiography profile of children with DCM
– At initial presentation

S.No	***Characters***	***Mean***	***SD***
1	Ejection fraction	31.24	5.05

2	LV EDD/ BSA	10.64	3.19
3	LV ESD/ BSA	8.81	2.67
4	LV PWT/ BSA	13.76	4.78
5	Fractional shortening	17.10	4.89
6	LVEDD/LVPWT	8.05	1.88

Table 5:
Echocardiography profile of children with DCM – At initial presentation

SI No	***Characters***		***Number***	***Percentage***	
7	LV diastolic dysfunction	Grade I	12	21.82	27.27
		Grade II	3	5.45	
8	Mitral regurgitation	Mild	18	32.73	65.46
		Moderate	16	29.09	
		Severe	2	3.64	
9	Pulmonary hypertension	Mild	4	7.27	21.82
		Moderate	5	9.09	
		Severe	3	5.45	
10	LV Clot Present		3	5.45	
11	Pericardial effusion		1	1.8	

All of them presented with left ventricular systolic dysfunction with depressed ejection fraction and fractional shortening. Left ventricular diastolic dysfunction was present in 27.27% of patients; it was grade I in 21.8% and grade II in 5.45%. Mitral regurgitation was present in 65% of them with varying severity. Intraventricular clot was present in 3 cases. (Table 5)

Table 6:
Echocardiographic profile of children with DCM - at last follow up

SI No	***Characters***	***Mean***	***SD***
1	Ejection fraction	46.10	13.04
2	LV EDD/ BSA	10.24	3.02
3	LV ESD/BSA	7.72	2.56
4	LV PWT/ BSA	14.53	5.05

5	Fractional shortening	25.01	7.43
6	LVEDD/LVPWT	7.27	1.44

Both ejection fraction and fractional shortening are improved on follow up. The follow up period ranges from 6 months to 21 months with a mean follow up of 7 months. (Table 6)
The following is the outcome of children with DCM

Table 7:
Outcome of children with DCM

SI No	***Parameters***	***Number***	***Percentage***
1	Improved	38	69.09
2	Not improved	6	10.91
3	Expired	11	20

38(69%) children showed clinical and echocardiographic improvement on follow up and in 4(7.2%) children all medications have been stopped. Among the 17, 11 children died and 6 children did not show significant clinical and echocardiographic improvement. Out of 11 children who died, 7 were during the first admission and the remaining within 6 months of presentation. (Table 7)
The following is the results of univariate analysis of various characters predicting the outcome of children with DCM

Table 8:
Factors predicting the outcome of DCM in children

Characters	***Total (N=55)***	***Not improved (N=17)***	***Improved (N=38)***	***OR***	***95% CI***	***P value***
	n(%)	***n(%)***	***n(%)***			
Age(<12mo)	23(41.8)	8(47.1)	15(39.5)	1.36	0.4,4.3	0.59
Preceding viral infection	14(25.5)	5(29.4)	9(23.7)	1.34	0.4,4.8	0.65
NYHA (class IV)	25(49)	14(82.4)	11(32.4)	9.8	2.3,41.1	0.0007
Family h/o DCM	3(5.5)	2(11.8)	1(2.6)	4.9	0.4,58.5	0.17
CCF	51(92.7)	17(100)	34(89.5)	0.66	0.5,0.8	0.16
CTR (>63%)	21(38.2)	12(70.6)	9(23.7)	7.7	2.1,27.9	0.0009
Pulmonary congestion	17(30.9)	12(70.6)	5(13.2)	15.8	3.9,64.5	0.00002
Chamber enlargement	10(23.3)	7(43.8)	3(11.1)	6.2	1.3,29.4	0.0143
ST-T changes	28(50.9)	14(82.3)	14(36.8)	2.6	0.6,12	0.2062
Low voltage complexes	10(18.2)	4(23.5)	6(15.8)	1.6	0.4,6.8	0.4916
Rhythm disturbances	11(20)	5(29.4)	6(15.8)	2.2	0.6,8.6	0.243
Coxsackie B positive	7(12.7)	3(17.6)	4(10.5)	1.8	0.4,9.2	0.4640
HIV positive	3(5.5)	1(5.9)	2(5.3)	1.12	.09,13.3	0.925

Table 8:
Factors predicting the outcome of DCM in children

Characters	***Total no***	***Not improved***	***Improved***	***OR***	***95% CI***	***P value***
	n (%)	***n(%)***	***N(%)***			
EF (<30%)	24(43.6)	12(70.6)	12(31.6)	5.2	1.5,18	0.0070
FS (<15%)	15(27.3)	11(64.7)	4(10.5)	15.6	3.7,66	0.00003
LVEDD/LVPWT (>8)	23(41.8)	17(100)	6(15.8)	0.26	0.13, 51	0.0000
LVDD	15(27.3)	11(64.7)	4(10.5)	15.6	3.7,65.5	0.00003
PHT	12(21.8)	8(47.1)	4(10.5)	7.5	1.8,30.8	0.0024
MR	18(32.7)	8(47.1)	10(26.3)	2.5	0.8,8.2	0.1297
LV clot	3(5.5)	3(17.6)	-	3.7	2.3,5.8	0.0077

Of the various demographic and clinical parameters NYHA class, cardiothoracic ratio, presence of pulmonary congestion, chamber enlargement on electrocardiogram are significantly associated with short term outcome on univariate analysis. Of the echocardiographic parameters all have significant associated with short term outcome except mitral regurgitation on univariate analysis. On multivariate analysis by multiple logistic regressions fractional shortening (P value 0.0018) and ratio of LV end diastolic dimension to posterior wall thickness (P value 0.0000) are the parameters having significant association with poor short term outcome (Table 8).

DISCUSSION

Dilated cardiomyopathy (DCM) is one of the most common causes of heart failure among children that is often progressive despite maximal medical therapy [21]. DCM constitutes the principal indication for pediatric cardiac transplantation [22].The epidemiology and clinical course of DCM in children are not well established and most children have an undiagnosed cause of DCM, which limits the potential for disease-specific therapies.

Age of presentation: about 42% of children were less than 12 months and 54.5% presented before their second birthday which is consistent with most published data. In a nationwide Finnish study carried out by Arola, et al, it was found that 52% of DCM occurs in the first year of life [11]. Also, Towbin, et al, reported a higher incidence in infants (<1 year) than in children [13]. In our study age at diagnosis is not significantly associated with outcome. Other studies have reported both for [12] and against [11] age as a prognostic indicator.

Sex of patients: In our study, 50.9% of patients were females and no predilection to sex was observed. In USA, the annual incidence was higher in boys than girls [13]. In the Finnish study 52% were males (4), 60.9% were males in the Indian study by Shyam S Kothari (12) showing a male preponderance whereas 65.5% were females in the Cairo study (20) and 54.7% females by Avezedo from Brazil (17). As with other studies gender has no significant association with outcome.

Family history: Three patients (5.45%) in our study group had familial cardiomyopathy. Similarly, Shyam S Kothari, et al, has reported 3.5% cases with familial DCM from AIIMS, India [12]. Anita Arola, et al [11] have reported 16% familial incidence whereas 14% has been reported in other studies [13, 14]. These shows possibly familial DCM is relatively uncommon in Asians [12]. It has no significant association with outcome.

History of preceding viral illness was present in 25.5% of cases and it has no association with outcome (p value 0.65). This is similar to the study by Shyam S Kothari, et al, [12] who has reported 30.5% and no significant association.

About 92.7% had congestive cardiac failure (CCF) at presentation with NYHA class III-IV. Anita khalit, et al from India has reported all patients presented with CCF [15]. NYHA class IV at presentation is significantly associated outcome. Similarly severity of symptoms at presentation has shown to be significantly associated with outcome in other studies [11, 13].

Cardiomegaly was present in all cases at presentation and the mean cardiothoracic ratio was 63±4.5 similar to other studies [11, 12, 20]. Higher cardiothoracic ratio (>63%) was found to be associated with poor outcome similar to AIIMS study [12].Pulmonary congestion was present in 30.9% of patients. It has significant association with outcome similar to the study by Anita Arola [11].

LVH by voltage criteria was present in 60% of cases and 18.18% had both LVH with LAE. 20% had some rhythm disturbances, 18% had low voltage complexes and 15% had nonspecific ST- T changes. Of all the parameters only combined LVH with LAE has come significantly associated with outcome. Anita Arola, et al [11] has reported only low voltage complexes had prognostic significance. Similar study from AIIMS has reported no prognostic significance with all ECG parameters [12].

Among serology for viral markers 12.7% came positive for coxsackie B virus and 5.5% for retro virus. Anita Khalil, et al from New Delhi has reported 16% coxsackie B and none with retroviral positive [15]. In our study both have no significant association with outcome. The diagnosis of postviral cardiomyopathy remains problematic. Studies have lent support to both immune and viral mediated cardiac damage after viral infection [17]. The persistence of viral RNA in the myocardium beyond 90 days by polymerase chain reaction, T- cell mediated immune responses in viral myocarditis, and apoptotic cell death all explain the pathogenesis of dilated cardiomyopathy following myocarditis [23]. Reasons for low ascertainment of viral illness projected earlier are due to collection of specimens well after the viremic phase of the initial illness, low utilization of early endomyocardial biopsy, and lack of

direct viral testing on myocardial samples, whereas over ascertainment may be due to spurious association with systemic viral illnesses[14].

Depressed left ventricular systolic function, measured by ejection fraction and fractional shortening, was present in all. Mean ejection fraction and fractional shortening at presentation were 31.24±5.05 and 17.1±4.89 respectively. At the end of the study it was 46.1±13.04 and 25±7.43.

Ejection fraction of <30% was found to have significant association with poor outcome. C J McMahon, et al [16] have reported left ventricular ejection fraction to be independent predictor of outcome. LV ejection fraction <30% had a 68% specificity and 74% sensitivity in predicting the death, hospitalization, transplant. Vitor Manuel Pereira Azevedo, et al [17] have concluded that reduced LV ejection fraction as a marker of death and a reduction in LV ejection fraction should be considered for early heart transplantation.

Fractional shortening was found to be independently associated with poor outcome in our study. The mean FS at presentation was 17.1±4.89 and it has increased to 25.01±7.43 among those who have improved. FS < 15% was significantly associated with poor outcome. Piers E. F. Daubeney, et al [14] in their study from Australia have reported lower initial fractional shortening z score, and failure to increase fractional shortening z score during follow-up are significant risk factors for death or cardiac transplant. Jeffrey A. Towbin, et al. [13] also have reported that higher fractional shortening z score was associated with better outcome and fractional shortening was the only independent echocardiographic risk factor.

Ratio of LV end diastolic dimension to posterior wall thickness was another parameter independently associated with outcome. Mean ratio at presentation was 8.05±1.88 and 7.27±1.44 among those who have improved. Shyam S Kothari, et al, [12] have reported a higher ratio of LVED/PW thickness was associated with a poor outcome. This ratio may indirectly reflect a preserved ventricular mass, although the values found in both groups were much higher than normal (3.4–3.8) [24].The ratio of LVED/PW thickness was also found to be a useful predictor by Carvalho et al. [25]. This index is independent of the age of the patients, and indirectly reflects the relatively preserved left ventricular mass. This index suggests that measures to increase the left ventricular mass may influence the course of DCM favorably. Significantly, the treatment of children with myocardial growth factors, such as growth hormone, has been reported [26]. Inas Abdullsattar Saad, [20] have also reported that higher LV Posterior wall thickness in diastole was significantly related to favorable outcomes.

LV diastolic dysfunction at presentation was also significantly associated with poor outcome. Rihal C S, et al, have concluded in their study that markers of diastolic dysfunction correlated strongly with congestive symptoms, whereas variables of systolic function were the strongest predictors of survival [27].

Presence of LV clot and need for anti coagulant therapy has significant association with outcome. Similarly a poor outcome was linked to the severity of heart failure at presentation and during follow-up, as indicated by need for anti coagulation therapy, by Anita arola, et al [11].

In our study mitral regurgitation has no significant association with outcome. This is similar to the other studies [11,12,13]. Vitor Manuel Pereira Azevedo, et al [17] has stated that progressive worsening of mitral regurgitation should be considered for early heart transplantation.

Outcome: In our study 38(69%) patients showed improvement to medical therapy which is similar to recently published results which showed 52.5% of patients recovered [28]. Out of the 17(30%) patients who did not improved, 11(20%) patients died and 6(10.9%) patients had persisting clinical symptoms or echocardiographic parameters on follow up. This is similar to the study done at AIIMS, New Delhi where 59% improved, 23% remained unchanged and 18% died [12]. In other studies, it has been reported that after a median follow-up period of 2.5 years, about one- third of patients fully recovered, 38% survived with left ventricular dysfunction, and 29.4% died, most in the first year of follow-up [29]. Similarly, other researchers have stated that 33% of DCM cases improve with signs of improvement seen in the initial six months and continued improvement over two years [30].

Thus, in the present study, it is found by univariate ordinal regression that the following are the risk factors associated with unfavorable short term outcome. These include

1. NYHA class IV at presentation
2. Cardio thoracic ratio > 63%
3. Presence of pulmonary congestion
4. LV and LA enlargement in ECG
5. Ejection fraction < 30%
6. Fractional shortening <15%
7. Ratio of LV end diastolic dimension to posterior wall thickness >8
8. LV diastolic dysfunction
9. Presence of pulmonary hypertension
10. LV thrombus and need for anticoagulants.

Table 9:
Risk Factors For Poor Short Term Outcome

Characters	*Total (N=55)*	*Not improved (N=17)*	*Improved (N=38)*	*OR*	*95% CI*	*P value*
	n (%)	*n (%)*	*n (%)*			
NYHA(class IV)	25(49)	14(82.4)	11(32.4)	9.8	2.3,41.1	0.0007
CTR (>63%)	21(38.2)	12(70.6)	9(23.7)	7.7	2.1,27.9	0.0009
Pulmonary congestion	17(30.9)	12(70.6)	5(13.2)	15.8	3.9,64.5	0.00002
LVH+ LAE	10(23.3)	7(43.8)	3(11.1)	6.2	1.3,29.4	0.0143
EF (<30%)	24(43.6)	12(70.6)	12(31.6)	5.2	1.5,18	0.0070
FS (<15%)	15(27.3)	11(64.7)	4(10.5)	15.6	3.7,66	0.00003
LVEDD/LVPWT (>8)	23(41.8)	17(100)	6(15.8)	0.26	0.13, 51	0.0000
LVDD	15(27.3)	11(64.7)	4(10.5)	15.6	3.7,65.5	0.00003
PHT	12(21.8)	8(47.1)	4(10.5)	7.5	1.8,30.8	0.0024
LV clot	3(5.5)	3(17.6)	-	3.7	2.3,5.8	0.0077

And by multiple logistic regressions it is found that fractional shortening <15% (P value 0.0018) and ratio of LV end diastolic dimension to posterior wall thickness >8 (P value 0.0000) are independent risk factors for poor short term outcome.

CONCLUSION

1. Dilated cardiomyopathy more commonly present in the first year of life than at older pediatric ages.
2. Dilated cardiomyopathy has no predilection to sex.
3. Congestive cardiac failure is the common presenting manifestation of dilated cardiomyopathy.
4. Infants commonly present with feeding difficulty and respiratory symptoms. Older children commonly present with effort intolerance and anasarca.
5. Definitive establishment of viral etiology remains difficult in our setup.
6. Familial dilated cardiomyopathy is identified only in 5% of our patients in contrast to higher incidence reported in western literature.
7. Cardiomegaly is present in all patients with dilated cardiomyopathy.
8. Electrocardiogram commonly showed features of chamber enlargement followed by non-specific ST-T changes, low voltage complexes and rhythm disturbances.
9. The diagnosis of dilated cardiomyopathy is primarily based on echocardiography.
10. Echocardiographic parameters of dilated chambers with global hypokinesia, left ventricular dysfunction with depressed ejection fraction and fractional shortening are seen in all patients with dilated cardiomyopathy.
11. Predictors of short term outcome on univariate analysis are:
    a) NYHA class IV at presentation
    b) Cardio thoracic ratio > 63% in chest radiograph
    c) Presence of pulmonary congestion
    d) Left atrial and left ventricular enlargement in electrocardiogram
    e) Ejection fraction < 30%
    f) Fractional shortening <15%
    g) Ratio of left ventricular end diastolic dimension to posterior wall thickness in diastole > 8
    h) Left ventricular Diastolic Dysfunction
    i) Presence of pulmonary hypertension
    j) Left ventricular thrombus and need for anticoagulants
12. Fractional shortening <15% and Ratio of left ventricular end diastolic dimension to posterior wall thickness in diastole >8 are the independent predictors for poor short term outcome on multivariate analysis.

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ANNEXURE

PROFORMA

Name: REG NO:
Age:
Sex:
Postal address:
Telephone number:
Father's name:
Mother's name:
Income :
Present complaints:
- Age at onset :
- Duration&Progression:
- H/O Preceding viral illness (Fever,Coryza,Gastroenteritis)
- H/O suggestive of complications

Past history:
- H/O first Hospitalization for similar illness
- H/O of subsequent admissions

- Medical treatment

Birth history:

Family history:
- H/O consanguinity
- H/O cardiac illness
- (Parental screening in necessary cases)

Examination:
- Anthropometry:

- Vital parameters:
- General examination:
  - Nutrition
  - Dysmorphism
  - Musculo skeletal defects
  - Pallor,cyanosis,clubbing
- Cardio vascular examination
- Other systems

Investigations:
- Chest radiograph
- ECG
- Echocardiogram
- Viral markers(Coksakie B,HIV)
- Serum calcium&phosphate

Treatment:

- Anti Failure drugs & dose
- Anti Arrthymic drugs
- Anti Coagulant drugs
- Carnitine therapy

Follow up

- I month
- III month
- VI month

COMPLAINTS

GENERAL & SYSTEMIC EXAMINATION

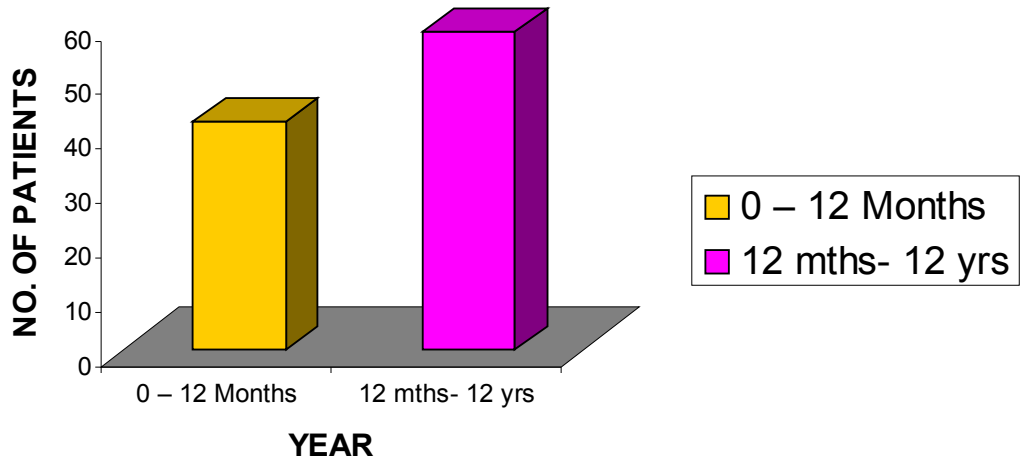
TREATMENT

ECHOCARDIOGRAM

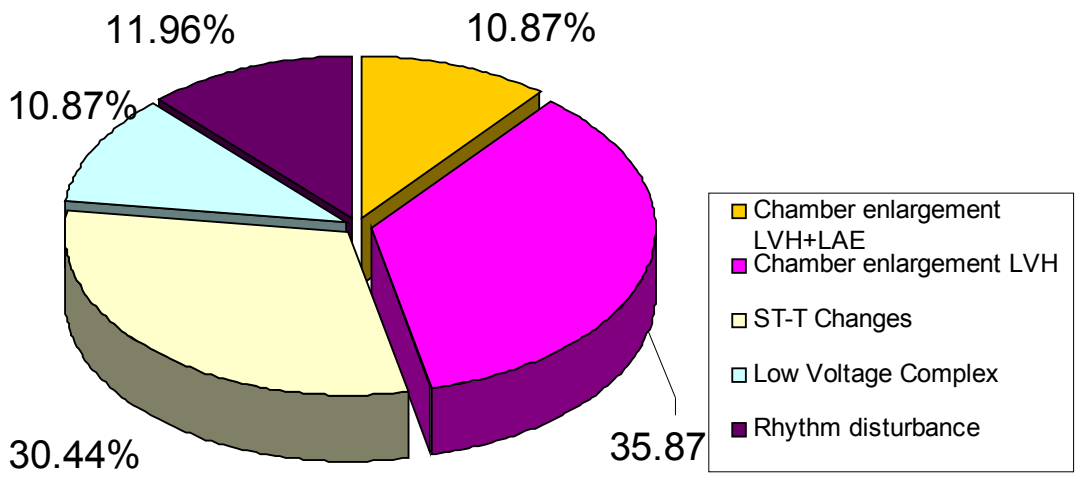
ABBREVIATIONS

ACE	– Angiotensin Converting Enzyme
AIIMS	– All India Institute Of Medical Sciences
ALCAPA	– Anomalous Left Coronary Artery Arising from Pulmonary Artery
BSA	– Body Surface Area
CCF	– Congestive Cardiac Failure
CI	– Confidence Interval
CTR	– Cardio Thoracic Ratio
DCM	– Dilated Cardiomyopathy
DNA	– Deoxy Ribo Nucleic Acid
ECG	– Electro Cardiogram
EDD	– End Diastolic Dimension
EF	– Ejection Fraction
ESD	– End Systolic Dimension
FS	– Fractional Shortening
HIV	– Human Immunodeficiency Virus
LA	– Left Atrium
LAE	– Left Atrial Enlargement
LV	– Left Ventricle
LVDD	– Left Ventricular Diastolic Dysfunction
LVH	- Left Ventricular Hypertrophy
MR	– Mitral Regurgitation
NYHA	– New York Heart Association
OR	– Odds Ratio
PCR	– Polymerase Chain Reaction
PHT	– Pulmonary Hypertension
PWT	– Posterior Wall Thickness
RNA	– Ribo Nucleic Acid
SD	– Standard Deviation
ST-T	– ST segment and T wave

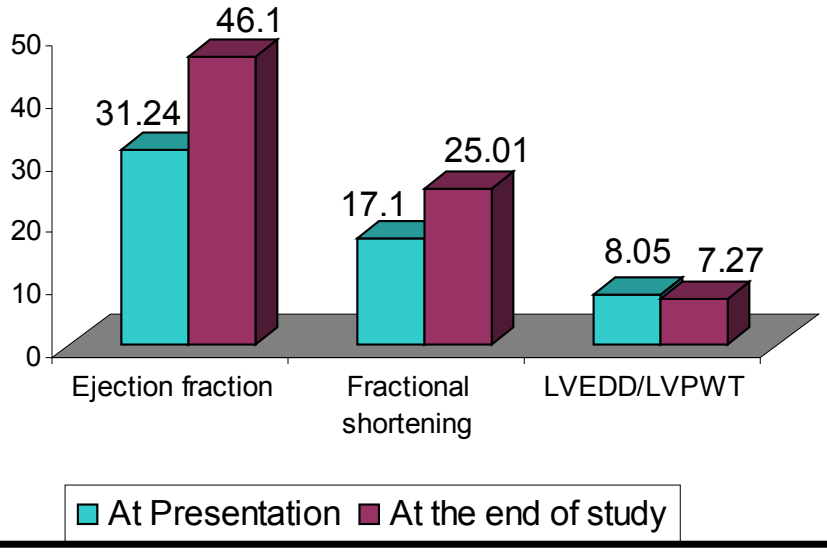
DILATED CARDIMYOPATHY - AGE OF PRESENTATION



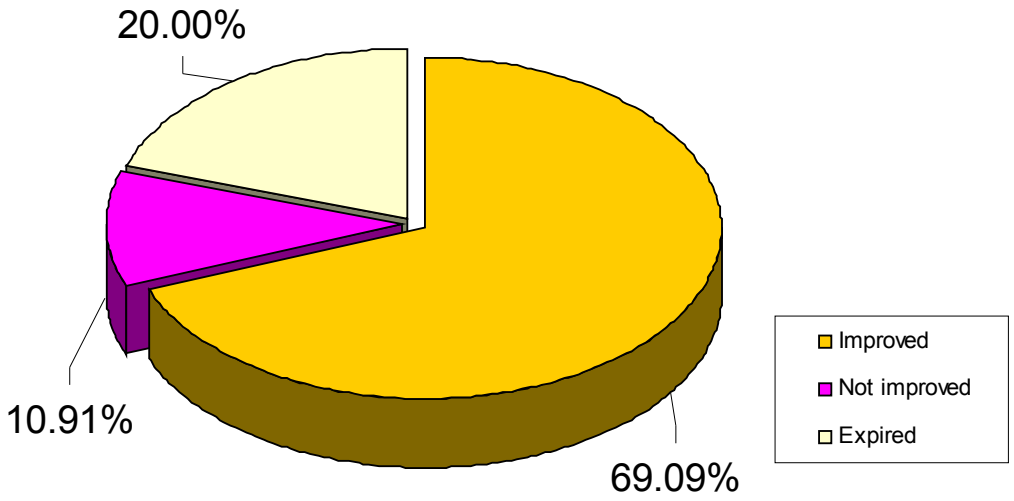
DILATED CARDIMYOPATHY - ECG CHANGES

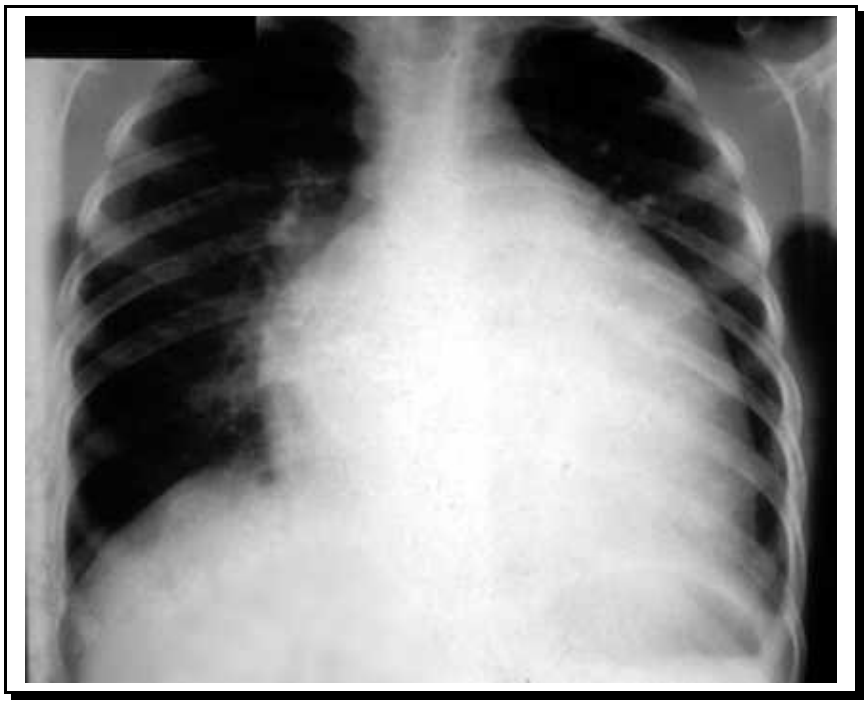


DILATED CARDIOMYOPATHY - ECHO PARAMETERS

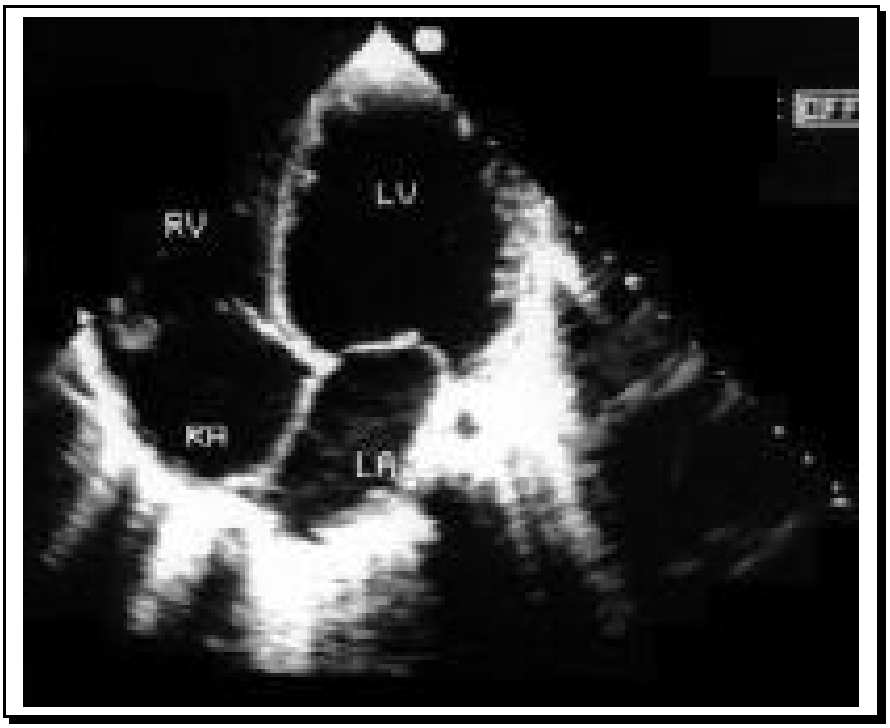


DILATED CARDIMYOPATHY - OUTCOME





DCM – CARDIOMEGALY



DCM - FOUR CHAMBER VIEW